REMARKS/ARGUMENTS

Applicant thanks the Examiner for the careful consideration given the present application, and respectfully submits that the application is allowable in view of the following remarks.

Claims 1-4, 6-34 and 71 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is explained in the Office action that the process for "selecting" a microorganism is not clearly delineated in claim 1. Further, the Office action points out that it is unclear how "an alternative oxidant" is identified for any and all microorganisms, the nature of which is not determined.

Contrary to the rejection set forth in the Office action, applicant respectfully submits that the language of claim 1, as amended, clearly explains how to select a microorganism according to the present invention. Any microorganism can be selected so long as it is "capable of utilizing oxygen or an alternative oxidant source other than oxygen for cellular respiration", and has "the ability to produce the desired biological product." It is well within the ability of one of ordinary skill in the art to select such a microorganism, especially in light of the disclosure of the present invention set forth in the specification.

Regarding the rejection of claim 1 for uncertainty surrounding how to identify a proper alternative oxidant source to supply to the culture medium for the selected microorganism, applicant notes that claim 1 has been amended to more clearly express this limitation. As amended, claim 1 now recites "supplying the culture medium with *the* alternative oxidant source". Without antecedent basis, the alternative oxidant source is the alternative oxidant source, other than oxygen, that can be utilized by the microorganism for cellular respiration recited earlier in the claim. Thus, there can be no confusion or uncertainty surrounding the selection of a microorganism and the identification of an alternative oxidant source. Accordingly, applicant respectfully submits that claim 1 particularly points out and distinctly claims the subject matter which applicant regards as the invention in compliance with 35 U.S.C. §112, second paragraph.

Claim 71 also complies with the requirements of 35 U.S.C. §112 for reasons analogous to those set forth above.

Claims 1-6, 10 and 16 are rejected under 35 U.S.C. §102(b) as being anticipated by Varma et al.1 However, applicant respectfully submits that Varma et al. fails to teach every feature of the present invention.

Varma et al. is directed to the growth of the microorganism E. coli in various culture conditions. The culture conditions discussed are aerobic chemostat, batch, fed-batch and anaerobic batch conditions. According to Varma et al., reconsumption of acetate was observed in the aerobic fed-batch cultures. Pg. 3730, second col., 3rd full paragraph. The aerobic fed-batch cultures were initiated by inoculating bacteria into defined mineral medium without a carbon source and continuously feeding glucose using a syringe pump to the culture as the carbon source. Gas sparging was performed with a small bubble size to keep dissolved oxygen above 50% saturation, and temperature regulation maintained the temperature at 38°C.

Varma et al. fails to teach supplying the culture medium with an alternative oxidant source, other than oxygen, as claimed in amended claim 1. The Office action explains that Varma et al. discloses "the production of cells of the microorganism E. coli in the presence of the alternative oxidant source acetate under aerobic conditions such that the strain uses the alternative oxidant source." However, the phrase "alternative oxidants" is defined according to the present invention as being selected from nitrates, nitrites, sulfates, sulfites, carbon dioxide or carbonates, bicarbonates, fumarates, sulfur, manganic ion, ferric ion, selenate, dimethyl sulfoxide, arsenate, trimethylamine-N-oxide and glycine.

Varma et al. also fails to teach maintaining the culture medium at a desired pH, as claimed in amended claim 1. As mentioned above, Varma et al. does suggest maintaining the temperature of the culture at 38°C, but Varma et al. is silent regarding pH, and maintenance of the pH.

Further, Varma et al. fails to teach allowing the culture medium to incubate for a time sufficient to produce a desired quantity of a biological product. Varma et al. is a study of the

accuracy of models to predict growth and metabolic by-product secretion rates. The study is not concerned with the production of a desired product, a quantity of the desired product that is to be produced, or incubating the culture medium for a sufficient time to produce this desired quantity. Accordingly, applicant respectfully submits that Varma et al. does not anticipate claim 1, as amended.

Regarding the rejection of claim 2 under §102(b) as being anticipated by Varma et al., applicant respectfully submits that isolating and recovering the desired biological product from the culture media is not taught by Varma et al. As previously mentioned, Varma et al. is not concerned with the production, quantity or recovery of a desired product. Varma et al. does not teach this feature and therefore, does not anticipate claim 2.

Claims 1-4, 6, 10, 13, 15, 17-20, 22, 27-29, 31-34 are rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 5,501,966 to Giani et al. Applicant respectfully submits, however, that Giani et al. fails to teach every feature of the present invention.

Giani et al. is directed to a process for the preparation of L-Rhamnose by fermentation of Pseudomonas aeruginosa (hereinafter "P. aeruginosa"). P. aeruginosa is fermented in a medium containing vegetable oils, one or more nitrogen sources, sulfate and magnesium ions and potassium and chloride ions, one or more phosphorus sources and trace elements. The pH of the nutrient solution should be between pH 5.5 and 7.5 at the start of fermentation, and does not need to be controlled during the course of the fermentation. Aeration is performed by blowing air into the stirred fermentation solution.

Giani et al. fails to teach maintaining the culture medium at a desired pH, as claimed in amended claim 1. According to Giani et al., the pH does not need to be controlled after being initially established to a desired pH at the start of the fermentation. This is further illustrated by the examples in Giani et al. In each of the examples, the pH is initially established at a desired value, and then ignored thereafter. Some of the examples further adjust the pH during a purification process, but again, the pH is initially established and then disregarded. In contrast, the present invention as claimed in claim 1, includes the step of maintaining the culture medium

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1 Varma, Amit and Palsson, Bernhard O., "Stoichiometric Flux Balance Models Quantitatively Predict Growth and Metabolic By-Product Secretion in Wild-Type Escherichia coli W3110", Applied and Environmental Microbiology, pp. 3724-3731 (Oct. 1994).

at a desired pH. As explained in the specification of the present application, the pH of the culture medium is maintained in an optimal range according to the present invention.

Further, Giani et al. fails to teach supplying an alternative oxidant source to the culture medium such that a portion of the microorganisms within the culture medium will utilize the alternative source for cellular respiration when the oxygen requirements for cellular respiration is greater than the maximum rate of oxygen supply to the culture medium, as claimed in amended claim 1. Giani et al. teaches blowing sterile air into the stirred fermentation solution for aeration purposes. Should the demand for oxygen exceed the available oxygen within the fermentation medium, the aeration rate can be increased by adjusting one or more of the fermenter geometry, the stirrer geometry, and the energy input. Increasing the aeration rate according to Giani et al. can cause the fermentation solution to foam, thus requiring an antifoam agent to be introduced into the fermentation medium. With the antifoam agent provided to allow a sufficient influx of sterile air into the fermentation medium, Giani et al. is silent about providing an alternate oxidant source such that a portion of the microorganisms will utilize the alternative oxidant source when the oxygen requirement for cellular respiration is greater than the maximum rate of oxygen supply to the culture medium. Accordingly, applicant respectfully submits that claim 1 is not anticipated by Giani et al.

Claims 1-4 and 6-34 also stand rejected under 35 U.S.C. §103(a) as being unpatentable over Giani et al. in view of Brock2 and U.S. Patent No. 4,814,272 to Wagner et al. Applicant respectfully submits, however, that the combination of references fails to teach every feature of the present invention. Specifically, the combination fails to teach maintaining the culture medium at a desired pH as discussed above with regard to Giani et al. The combination also fails to teach supplying an alternative oxidant source to the culture medium such that a portion of the microorganisms within the culture medium will utilize the alternative source for cellular respiration when the oxygen requirements for cellular respiration is greater than the maximum rate of oxygen supply to the culture medium, for reasons analogous to those discussed above. The detailed remarks discussed above are not reproduced here.

Further with regard to the rejection of claims 1-4 and 6-34 as being unpatentable over Giani et al. in view of Brock and Wagner et al., applicant respectfully submits that the references

2 Brock, Thomas D., Biology of Microorganisms, Prentice-Hall, Inc., pp. 113-114 (3d ed., 1979)

lack sufficient motivation therein to justify their combination. Obviousness can only be established by combining the teachings of the prior art to produce the claimed invention where there is some suggestion or motivation to do so. *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988); MPEP 2143.01. The prior art must also suggest the desirability of the claimed invention. MPEP §2143.01. Prior art references must be considered in their entirety, including disclosures that teach away from the claims. MPEP §2141.02. Further, the proposed modification cannot render the prior art unsatisfactory for its intended purpose or change the principle of operation of a reference. MPEP §2143.01.

In light of the discussion above, Giani et al. teaches away from the present invention by teaching that the pH is not controlled in the course of the fermentation. This is in direct contrast to claim 1, which recites the step of maintaining the culture medium at a desired pH.

Giani et al. goes on to disclose that an antifoam agent is added during fermentation to prevent the formation of foam, presumably caused by stirring of the fermentation solution. Applicant notes that the disclosure of the present application explains that known anti-foam agents are very expensive, and may affect cell metabolism, downstream product recovery and purification, and wastewater processing. The present invention provides an alternative to vigorous agitation, and associated problems, for satisfying the requirements for cellular respiration. Accordingly, applicant respectfully submits that the references teach away from the present invention, and thus, lack sufficient motivation to justify their combination.

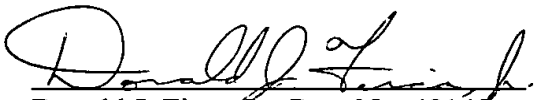
Further yet, the combination of the references would change the principle of operation of the prior art invention being modified. As the previous paragraph explained, aeration was accomplished in Giani et al. by blowing sterile air into the stirred fermentation solution. The amount of oxygen required for cellular respiration is satisfied by varying the aeration rate. Like Giani et al., Wagner et al. is directed toward an aerobic process that does not make use of an alternative oxidant source for cellular respiration. In contrast, Brock lists several oxidant sources for anaerobic respiration. Thus, the combination of Brock with Giani et al. and Wagner et al. would change the principle operation of Giani et al. and Wagner et al. from aerobic respiration to a combined aerobic/anaerobic cellular respiration. Accordingly, applicant respectfully submits that claims 1-34 are patentable over Giani et al. in view of Brock and Wagner et al.

In view of the Amendments and the discussions presented above, reconsideration and withdrawal of all the rejections is respectfully requested. The claims should now be in a condition for allowance, and notice to that effect is also requested.

In the event that minor issues remain unresolved, the Examiner is requested to contact the undersigned to arrange for a telephone interview to expedite disposition of this application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 500959 (089498.0338) for any additional fees required under 35 C.F.R. §1.16 or 1.17.

Respectfully submitted



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